Biomedical Concepts
Diagnosis ◆ Evaluation ◆ Education ◆ Research
Carlos Bedrossian, M.D., Ph.D. (Hon.) Ph. (708) 445-9691 Fax (708) 445-9692
715 Lake St., Ste. 500, Oak Park, IL 60301 Carlos@Biomedical-Concepts.com

March 18, 2016 Sent via email

Ms. Jeannette Davis
Motley Rice, Attorneys at Law
28 Bridgeside Blvd
Mr. Pleasant, SC 29464

Re: John Haskins

Dear Jeannette:

Thank you for the opportunity to review the pathology materials from the above-captioned individual, an 80 year old man who was diagnosed with malignant mesothelioma (MM) in November of 2014. At your request, I reviewed Mr. Haskins' work history and evaluations for occupational lung disease, as well as the results of laboratory tests, radiological examinations, and ancillary procedures which assisted his treating physicians in providing his medical care. I also reviewed admission entries, discharge summaries, progress notes from clinical visits and other medical records connected to Mr. Haskins' hospitalizations at Brigham & Women's Faulkner Hospital in Boston, MA. In addition I reviewed outpatient medical records from visits to Dana Farber Cancer Institute at Brigham & Women's, where Mr. Haskins saw primarily clinical and surgical oncologists. Finally, I reviewed Mr. Haskins's pathology slides and corresponding reports from his biopsy procedures. Finally, I also reviewed pathology slides and corresponding reports from Mr. Haskins' biopsy procedures upon which his cancer diagnosis was based and correlated the findings with his clinical condition. In reaching my conclusions, I relied upon the peer-reviewed medical literature, as well as my education, knowledge, and experience developed over more than forty years in the practice, teaching and research on pulmonary pathology.

Mr. Haskins served in the US Navy from January of 1953 until July of 1956 as a fireman and engine room man aboard the USS Coney. The ship underwent a major overhaul during the time Mr. Haskins was stationed aboard. He remained on the ship during the entire time of the overhaul to maintain the engine room equipment. The mechanic from the Charleston Naval Shipyard carrying out the overhaul removed and installed asbestos-containing material (ACM) in the engine room and throughout the ship. Mr. Haskins worked alongside these mechanics in the confined space of the ship. Once the overhaul was complete and the ship set sail, Mr. Haskins operated, repaired, and maintained the engine room machinery and equipment, which included turbines, condensers, evaporator, pumps, and valves.

Asbestos-insulated areas of a ship include the hull, decks, superstructure, cargo gear, and smoke stack. Seamen who performed maintenance responsibilities sustained direct, heavy exposure to asbestos since asbestos insulation covered all of the piping, equipment and

machinery operated and maintained on a daily basis. Seamen like Mr. Haskins had significant direct and bystander exposure to asbestos through their direct duties or while working alongside other seaman as they shared the confined shipboard environment with crewmen who handled asbestos-containing materials on a daily basis. Whenever Mr. Haskins worked in the engine room, he sustained direct, heavy asbestos exposure from ACM of various ship components.

As he worked with and around asbestos hands-on, or close to others handling ACM, Mr. Haskins routinely found himself in areas where visible dust was generated. Unfortunately, aerodynamic asbestos dust particles contain aerosolized asbestos fibers suspended in the air. Under these conditions of visible atmospheric dust, Mr. Haskins was regularly exposed to high levels of asbestos fibers while aboard ship. On these occasions, it was a common occurrence for Mr. Haskins to have his garments and equipment covered in dust at the end of his working day.

While working directly with asbestos-containing products or in the close proximity of others doing so, there is no indication Mr. Haskins routinely wore a mask, a respirator or any other type of respiratory protection. As a consequence of these physical conditions, he could not help but breathe an atmosphere of airborne asbestos fibers in his immediate workspace, which he inhaled into his lungs. Mr. Haskins' smoking history is unclear. There is no indication he abused alcohol or illegal drugs.

Mr. Haskins' medical history includes diabetes, atrial flutter, pace maker, and hypertension. On March 25, 2013, he was being evaluated for spinal disease, when a chest x-ray incidentally revealed a right pleural effusion and coarse calcifications in the upper zones bilaterally. The effusion was again noted on an April 2nd study, and an April 23rd CT chest scan, which also noted bilateral calcified pleural plaques, possibly related to asbestos exposure. The plaque was particularly heavy at the right lung base. On May 6, 2013, Mr. Haskins underwent an ultrasound-guided right thoracentesis, with 100 mL of clear, yellow fluid removed. The pathology sample **(S13-3878)** contained clusters of atypical mesothelial cells suspicious for mesothelioma. Immunostaining was positive for WT-1, Calretinin, and was negative for CEA and TTF-1. The cytology sample **(C13-9630)** was also suspicious for mesothelioma.

Because no cancer cells were found during the March 25th procedure, there was no follow-up with a thoracic surgeon at that point. But on June 18, 2013, Mr. Haskins presented to the emergency room with signs of a possible stroke. A June 21st study continued to demonstrate the layering right pleural effusion and calcifications at the lung apices consistent with pleural plaque. Over the next year, Mr. Haskins was monitored closely for recurrent disease. On November 19, 2014, he saw his physician for sudden hearing loss in his right ear, but again, he was found to have a large right pleural effusion. He underwent another thoracentesis on the 19th, with 1.1 L of pleural fluid removed. The pathology sample **(S14-10004)** was positive for malignant mesothelioma, with immunostaining positive for WT-1 and Calretinin, and negative for CEA. The cytology sample **(C14-2696)** was examined via a cytogenetic study, which revealed that eight of nine metaphases from the pleural fluid contained clonal aberrations that included several losses/deletions (3p, 6q, and 22q) typically found in malignant mesothelioma. The procedure resolved the effusion completely.

During a follow-up outpatient visit on December 19, 2014, Dr. Michael Rabin noted Mr. Haskins' asbestos exposure in the US Navy. A staging CT scan that day showed recurrence of the right pleural effusion and the persistent pleural plaques. Dr. Rabin described Mr. Haskins' disease as low volume malignant mesothelioma. Mr. Haskins was feeling fairly well and did not wish to pursue aggressive measures at that point, opting for symptom management. He consulted with Dr. Raphael Bueno at the Dana Farber Cancer Center on December 22, 2014 for treatment options. He had catheter placement for his recurrent effusion. Radiography continued to show effusion recurrence.

Mr. Haskins' June 29, 2015 chest x-ray right perihilar ground glass opacity. A July 1st study also noted nodular opacities throughout the right lung, greatest in the upper lobe. Catheter placement improved his symptoms greatly. A November 19, 2015 chest x-ray still identified the right lung base opacity and bilateral pleural calcifications. As of the present, Mr. Haskins is stable and is closely monitored for management and disease progression.

I had the opportunity to examine an original H&E stained section of the cell block labeled S-14-10004 and C-14-2696 from the respective thoracenteses on May 6, 2013 and November 19, 2014. The sections contain a crowded, single cell population composed of an exceedingly high number of epithelioid tumor cells, present mainly as cohesive groups with rare discrete elements all sharing the same mesotheliomatous phenotype. Arranged mostly as knobby cellular aggregates and solid cellular spheres, the tumor cells also form occasional gland-like acini and rudimentary tubulopapillary structures with a fibrovascular core. Seen against a background of fibrin and lymphocytes, the malignant cells display cytological features denoting their mesothelial origin, including ruffled cell borders, dense cytoplasm, peripheral vacuolization, bridgeless intercellular spaces, and mildly atypical nuclei with occasional mitotic figures. The absence of an extraneous proliferating cell population starkly distinct from their neighbors reinforces the clinical-pathological findings showing that Mr. Haskins did not suffer from metastatic adenocarcinoma. Studding of the parietal pleura verified that these cyto-histological features were consistent with malignant mesothelioma, epithelioid type.

When contemplating a cytological diagnosis of malignant mesothelioma supported by clinical-radiological features, it is important to establish whether or not the proliferating cell population under scrutiny exhibits the mesotheliomatous phenotype. For this reason, I submitted unstained sections from the aforementioned cell block S-14-1004 for additional immunohistochemical staining with a panel of antibodies in order to characterize further the nature of Mr. Haskins' neoplasm. With appropriate controls, the tumor cells gave a positive reaction for D2-40, β-Catenin, and Cam 5.2, but negative for TTF-1. Together with the immunoprofile obtained at Faulkner Hospital; positive for Calretinin and WT-1 and negative for TTF-1 and CEA, these results add further weight to the diagnosis of malignant mesothelioma, corroborated also by the radiological findings and the clinical impression of his treating physicians.

Asbestos exposure carries an increased risk for the development of both benign and malignant asbestos-related lung diseases. As reviewed elsewhere, asbestos, a unique fiber with numerous industrial applications, is also a potent lung cancer-inducing agent and the most common cause of MM, a link which has been well established for the last half century (**Bedrossian, 1992**). Asbestos exposure has been classified as a known carcinogenic event not only in the medical and scientific literature, but also in a number of publications emanating from

national and international health organizations, as well as regulatory agencies including but not limited to: the U.S. Environmental Protection Agency (**EPA, 1984**), the National Toxicology Program of the U.S. Department of Health and Human Services (**NTP, 2005**), and the International Agency for Research on Cancer (**IARC, 1998**). Despite asbestos warnings and the banning of asbestos use in many industrialized nations, an estimated 2,000-2,500 deaths/year from MM still occur and are related to asbestos exposure in the United States alone (**O'Reilley, 2007**).

While varying in potency, all fiber types including amphiboles and chrysotile cause lung cancer and MM, and as such should be treated with the same level of concern due to their well-established carcinogenicity **(Stayner, 1996**). Once inhaled, asbestos fibers cause alveolar epithelial cell injury by the release of reactive oxygen species (**Broaddus, 1996)** and triggering specific signaling pathways that regulate the production of cytokines and growth factors by mesothelial and other target cells in the lung (**Kamp, 2009**). Although pleural MM is by far the most common type of this condition, a similar mechanism operates upon contact of asbestos fibers with cells in any of the three major serosal cavities.

Inhaled asbestos fibers migrate from the lung parenchyma to the pleura and peritoneum via lymphatics (**Suzuki, 1991).** Upon entering the pleural cavity asbestos tumorigenesis is enhanced by at least six separate mechanisms: 1) Irritation of the pleura leading to chronic inflammatory process characterized by repeated cycles of damage and repair, during which reactive oxygen species (ROS) are generated and cause the release of cancer inducing cytokines, 2) mechanical entanglement with the process of mitosis by disrupting the mitotic spindle, 3) action of the ferritin heavy chain in iron as an anti-apoptotic protein during asbestos oxidative stress and as a catalyst in the formation of ROS, 4) induction of phosphorylation by mitogen activated protein kinases leading to persistent kinase-mediated signaling and unrelenting mesothelial cell proliferation, 5) interference with the telomerase mechanism enabling replicative immortality of tumor cells and 6) participation of asbestos in molecular carcinogenesis, by activating certain oncogenes, while blocking tumor suppressor genes **(Chua, 2009).**

Asbestos fibers cause target cell death in vitro, but through the above captioned mechanisms they become immortalized in vivo and continue to proliferate. The increased number of surviving cells constitutes the source of malignant neoplasms due to activation of the AP-1 pathway which induces neoplastic cell division, and secretion of TNF-Alpha and its receptors by macrophages and mesothelial cells **(Carbone & Bedrossian, 2006)**. This neoplastic proliferation escapes any attempt to stop it from all known natural defense mechanisms. The result is a lethal neoplasm, incurable due to its resistance to any form of therapy.

Most cases of MM occur in occupational groups subjected to "downstream exposure" in trades that include working in the construction, oil, chemical, steel, railroad, automotive, power plant, and shipbuilding industries (**Bedrossian, 2006**). Not only do these occupations entail significantly high levels of exposure to asbestos, but they also lead to increased concentrations of fibers in the lung of exposed individuals (**Barbieri, 2010**). MM constitutes an occupational health sentinel event, implying that the tumor was recognized as related to asbestos exposure over thirty years ago **(Rutstein, 1983**).The tumor is also considered a signal tumor, caused almost exclusively by occupational asbestos exposure (**Garcia, 2003**). Although there are other rare causes of MM, (e.g. radiation, thorotrast, empyema, erionite) none of them were documented in Mr. Haskins' case. In contrast, Mr. Haskins asbestos exposure as a service man in

the U.S. Navy who routinely handled ACM placed him among individuals at a high risk for the development of MM from the occupational exposure to asbestos in the work environment **(Lemen, 2011).**

The above occupations not only entail significantly high levels of exposure to asbestos, they also lead to increased concentrations of fibers in the lung of exposed individuals. In a tissue burden study, the average number of asbestos fibers in the lung was 105 x 10^6 fibers/dry gram in the lung and 49.8 x 10^6 fibers/dry gram in the serosal tissues, whether pleura or peritoneum **(Suzuki, 2001)**. Chrysotile, however, is rapidly cleared from the lungs and preferentially concentrated in serosal tissues where it exerts its carcinogenetic effect. Parenchymal retention of fibers, therefore, is not a good indicator of fiber burden in the pleura and peritoneum **(Smith & Griffin, 1996).** In addition, Suzuki's studies showed considerable variation in both the parenchymal retention and the serosal migration rates of fibers, indicative of variable individual resistance and susceptibility to the carcinogenic assault.

MM is invariably a lethal neoplasm, currently incurable by any known form of therapy, regardless of nature of the ACM releasing airborne asbestos or the fiber type responsible for its development **(Cullen, 1998)**. The ensuing malignancy is invariably the result of repeated, routine and direct handling of ACM, to fulfill the "frequency, regularity and proximity" test, or of being present in close vicinity of others doing so over a period time which may vary according to the individual susceptibility of the exposed person. The carcinogenic effect of asbestos is cumulative, regardless of the source of the exposure, which can be occupational, non-occupational or environmental in nature (**Hammar, 2008**). Total cumulative dose has been consistently found to be the best indicator of risk, and dose-response seemed to be expressed best by a "Cumulative Exposure Index" (**Iwatsubo, 1998).** However, one must take into account a variety of host factors, including genetic make-up, which influence the individual susceptibility to the development of mesothelioma secondary to asbestos exposure **(Becklake, 1991).**

Veterans who served in the U.S. Navy or the Coast Guard are known to undergo considerable asbestos exposure both aboard ship and ashore. Ship motion and vibration can release asbestos from gaskets, pipes, valves and other machinery in the surrounding space of seagoing vessels. In our experience and that of other observers, both benign and malignant asbestos-related lung disease are increased among U.S. Navy veterans particularly those serving at sea **(Jones, 1994**; **Selikoff, 1990; Kelman, 1990; Myers, 1991; Greenberg, 1991**). A link between MM and serving aboard ship has also been documented among veterans from the navies of several large maritime nations such as the United Kingdom (**Brims, 2009**), Norway (**Strand, 2010**), and Australia (**HNE.SO, 2012).** A similar trend exists among seamen in general, regardless of their civilian trade or military rank. Accordingly, a cohort study of Danish seafarers demonstrated an increased number of MM linked to asbestos exposure **(Kaerlev, 2005)**. Another cohort study of over thirty thousand Finnish seafarers detected an increased risk of malignant mesothelioma related to asbestos exposure aboard ship, particularly among deck personnel **(Saarni, 2002)**. Similar observations were published in studies from a number of maritime countries; Italy **(Bianchi, 2005),** Sweden **(Hemminki, 2003; Forsell, 2007),** Greece **(Varouchakis, 1991),** Norway **(Langard, 1994),** Denmark **(Brandt, 1994),** Iceland **(Rafnsson, 2003),** Japan **(Hiraoki, 2001)**, Korea **(Lee, 1999),** and Finland **(Pukkala, 1996).**

The above constellation of clinical, radiological and pathological findings is consistent with the view that Mr. Haskins suffered from MM. This type of cancer is known to occur in

individuals exposed to asbestos. It is therefore my medical opinion that Mr. Haskins contracted his occupational form of cancer following asbestos exposure in the US Navy. Not only his work history and latency period, but also the clinical presentation and evolution of his malignant neoplasm are all consistent with previous examples of asbestos-related lung cancer reported in the literature. It is also my conclusion, within a reasonable degree of medical probability, that Mr. Haskins' total and cumulative exposure to asbestos, from any and all products, containing any and all fiber types was a significant contributing factor to his risk of premature death from complications of his asbestos-related cancer.

I appreciated the opportunity to participate in the evaluation of Mr. Haskins' medical condition and its causation. To that end, I am returning all pathology materials and have retained the medical records for future reference. I reserve the right to further supplement or amend my report based on any new or additional information I receive. Please let me know if you have any questions.

I hereby declare under penalty of perjury that the factual statements in the foregoing report are true and correct to the best of my knowledge, information, and belief. I further certify that all of my opinions stated herein are held to a reasonable degree of medical certainty.

Sincerely,

Carlos WM. Bedrossian, MD
Consulting Pathologist
EIN: 20-4663234

References

1. **Bedrossian CWM**. Asbestos-related diseases: A historical and mineralogical perspective. *Sem Diagn Path,* 9(2):91-96, 1992.
2. U.S. Environmental Protection Agency. *Health Effects Assessment for Asbestos.* EPA/540/1-86/049 (NTIS PB86134608), 1984.
3. National Toxicology Program. Asbestos. In: *Report on Carcinogens. Eleventh Edition.* U.S. Department of Health and Human Services, Public Health Service, National Toxicology Program, 2005.
4. International Agency for Research on Cancer. *Asbestos. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 14. Lyon, France, 1998.
5. O'Reilly KM, Mclaughlin AM, Beckett WS, Sime PJ. Asbestos-related lung disease. *Am Fam Physician,*75(5):683-688, 2007.
6. Stayner LT, Dankovic DA, Lemen RA. Occupational exposure to chrysotile asbestos and cancer risk: a review of the amphibole hypothesis. *Am J Public Health*, February, 86(2): 179–186, 1996.
7. Broaddus VC, L Yang LM Scavo J D Ernst & Boylan AM. Asbestos induces apoptosis of human and rabbit pleural mesothelial cells via reactive oxygen species. *J Clin Invest,* 98(9), 2050–2059, 1996.
8. Kamp DW. Asbestos-induced lung diseases: an update. *Translational Res,* 153(4):143-52, 2009.
9. Suzuki Y & Kohyama N. Translocation of inhaled asbestos fibers from the lung to other tissues. *American journal of industrial medicine*, 19(6), 701-704, 1991.
10. Chua TC, Yan TD & Morris DL. Peritoneal mesothelioma: current understanding and management. *Canadian Journal of Surgery*, 52(1), 59, 2009.
11. Carbone M, **Bedrossian CWM.** The Pathogenesis of MM. *Sem Diagn Pathol,* 23:56-60, 2006.
12. **Bedrossian CWM.** Introduction: MM-New Tools, Same Dilemmas. *Sem Diagn Pathol,* 23:1-3, 2006.
13. Barbieri PG, Somigliana A, Festa R, Bercich L. Pulmonary concentration of asbestos fibers in steel workers with pleural mesothelioma. *G Ital Med Lav Ergon,* 32(2):149-153, 2010.
14. Rutstein DD, Mullan RJ, Frazier TM, Halperin WE, Melius JM & Sestio JP. Sentinel Health Events (occupational): a basis for physician recognition and public health surveillance. *Amer J of Public Health,* 73(9), 1054-1062, 1983.
15. García AM, Checkoway HA. Glossary for research in occupational health. *J Epidemiol Community Health,* 57:7–10, 2003.
16. Lemen R. Epidemiology of asbestos related diseases and the knowledge that led to what is known today. Chapter 5 in Dodson & Hammar's*: Asbestos: Risk Assessment, Epidemiology and Health Effects.* CRC-Press, Boca Raton, FL, 179-180, 2011.
17. Suzuki Y & Yuen SR. Asbestos tissue burden study on human malignant mesothelioma. *Industrial health*, 39(2), 150-160, 2001.
18. Smith AH & Griffin CC. Chrysotile asbestos is the main cause of pleural mesothelioma. *American journal of industrial medicine*, 30(3), 252-266, 1996.
19. Cullen MS. Chrysotile asbestos: enough is enough. *Lancet,* 351(9113), 1377-1378, 1998
20. Hammar SP, et al. Neoplasms of the Pleura Chapter 43 in Tomashevsky, et al (Editors). *Dail & Hammar's Pulmonary Pathology, Vol II, Neoplastic Lung Disease,* 3rd edition, Springer, London, 587-588, 2008.

21. Iwatsubo Y, Parion JC, Boutin C, Menard O, Massin N, Caillaud DP. Pleural mesothelioma: dose-response relation at low levels of asbestos exposure in a French population-based case-control study. *AmerJ of Epidemiology,* 148(2), 133-142, 1998.
22. Becklake MR. The epidemiology of asbestosis. *Mineral fibers and health*, 103-119, 1991.
23. Jones RN, Diem JE, Ziskand. MM, Rodregues M, Weill H. Radiographic evidence of Asbestos effects in American marine engineers. *J Occup Med,* 26☹4), 281-284, 1984.
24. Selikoff IJ, Lilis R, Levin G. Asbestotic radiological abnormalities among United States merchant marine seamen. *Br J Ind Med,* 47(5): 292–297, 1990.
25. Kelman HR & Kavaler F. Mortality patterns of American merchant seamen, 1973-1978. *American journal of industrial medicine,* 17(4), 423-433, 1990.
26. Myers JE. Merchant marine is not such a strange place for asbestos exposure. *Am J Ind Med,* 21)3):457, 1991.
27. Greenberg M. Cancer mortality in merchant seamen. *Annals of the New York Academy of Sciences,* 643(1):321-332, 1991.
28. Brims FJH. "Asbestos - a legacy and a persistent problem." *Journal of the Royal Naval Medical Service,* 95.1:4, 2009.
29. Strand LA, Martinsen JI, Koefoed VF, Sommerfelt-Pettersen J, Grimsrud TK. Asbestos-related cancers among 28,300 military servicemen in the Royal Norwegian Navy. *Am J Ind Med,* 53(1):64-71, 2010.
30. HNE, SO. DI (N) PERS 32-1 Royal Australian Navy Asbestos Management Plan (2012).
31. Kaerlev L, Hansen J, Hansen H, and Nielsen P. Cancer incidence among Danish seafarers: a population based cohort study. *Occup Environ Med,* 62(11), 761–765, 2005.
32. Saarni H, Pentti J, and Pukkala E. Cancer at sea: a case-control study among male Finnish seafarers. *Occup Environ Med,* 59(9): 613–619, 2002.
33. Bianchi C1, Bianchi T, Grandi G. Malignant mesothelioma of the pleura among seafarers. *Med Lav*, 96(6):490-495, 2005.
34. Hemminki K & Li Z. Time trends and occupational risk factors for pleural mesothelioma in Sweden. *J of Occup & Environ Med,* 45(4):456-461, 2003.
35. Forsell K, Hageberg S & Nilsson R. Lung cancer and mesothelioma among engine room crew – case reports with risk assessment of previous and ongoing exposure to carcinogens. *Int Marit Health,* 59(104), 5-13, 2007.
36. Varouchakis G, Velonakis EG, Amfiochiou S, Trichopoulos D. Asbestos in strange places: Two case reports of mesothelioma among merchant seamen. *Am J Ind Med,* 19(5):673, 1991.
37. Langard S. Prevention of lung cancer through the use of knowledge on asbestos and other work-related causes – Norwegian experiences. *Scandinavian journal of work, environment & health.* 100-107, 1994.
38. Brandt LPA, Kirk NU, Jensen OC & Hansen HL. Mortality among Danish merchant seamen from 1970 to 1985. *Amer J Ind Med,* 25(6), 867-876, 1994.
39. Rafnsson V, Sulem P. Cancer incidence among marine engineers, a population-based study (Iceland). *Cancer Causes & Control,* 14(1):29, 2003.
40. Hiraoka T, Watanabe A, Usuma Y, Mori T, Kohyama N, Takata A. An operated case of lung cancer with pleural plaques: its asbestos bodies, fiber analysis and asbestos exposure. *Ind Health,* 29, 194, 2001.
41. Lee KH, Yoon HS, Choi SJ & Kang D. Asbestos and exposure and malignant mesothelioma in Korea. *Asian Pac J Cancer Prev,* 10, 707-710, 2009.
42. Pukkala E & Saarni H. Cancer incidence among Finnish seafarers. *Cancer Causes & Control,* 7(2), 231-239, 1996.

Radiography

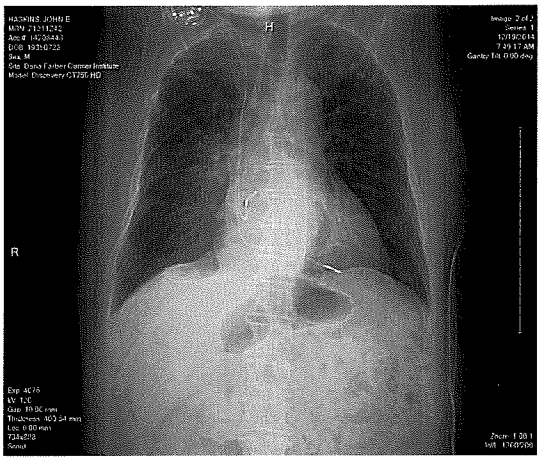

Fig. 1 – Xray 1

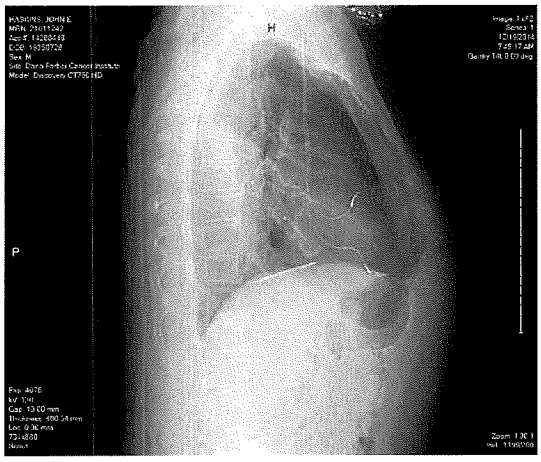

Fig. 2 – Xray 2

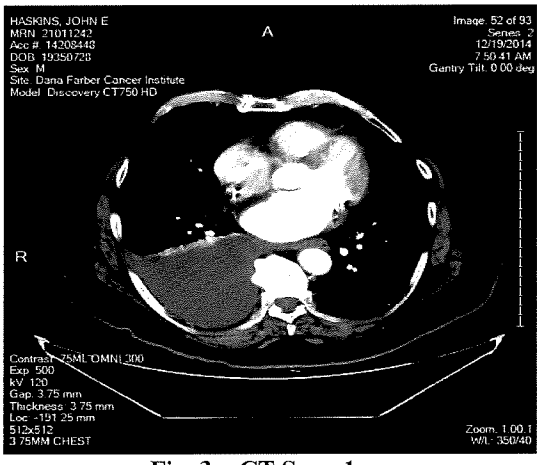

Fig. 3 – CT Scan 1

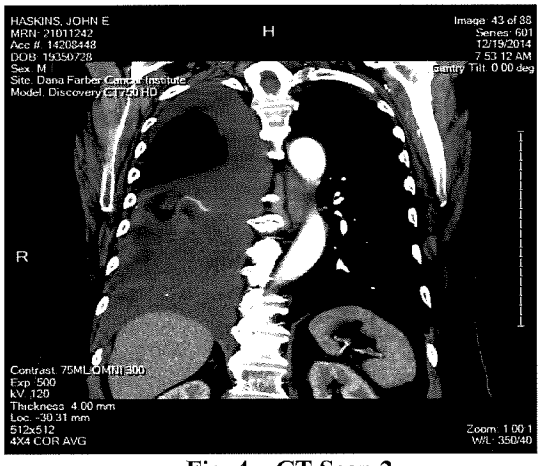

Fig. 4 – CT Scan 2

Illustrations

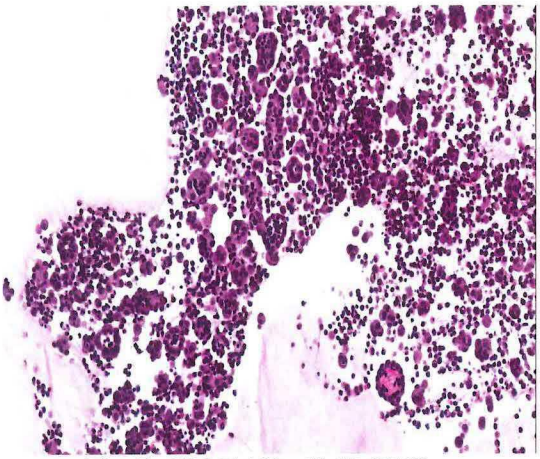

Fig. 5 – H&E 180x (S-13-3878)

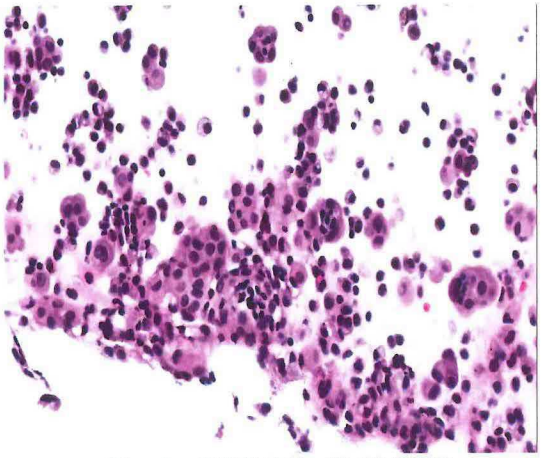

Fig. 6 – H&E 360x (S-13-3878)

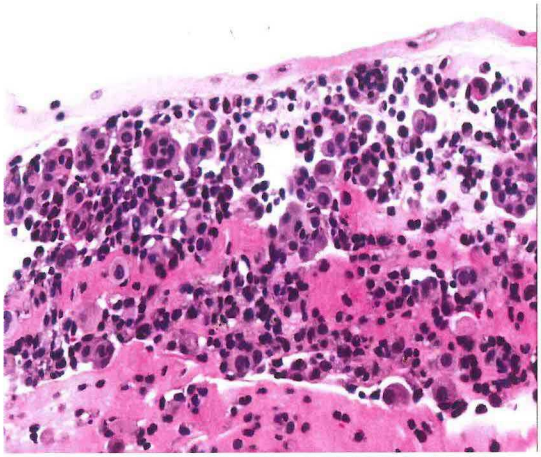

Fig. 7 – H&E(2) 360x (S-13-3878)

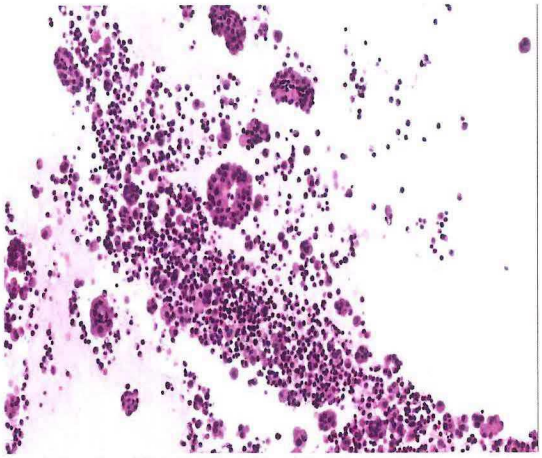

Fig. 8 – H&E(2) 180x (S-13-3878)

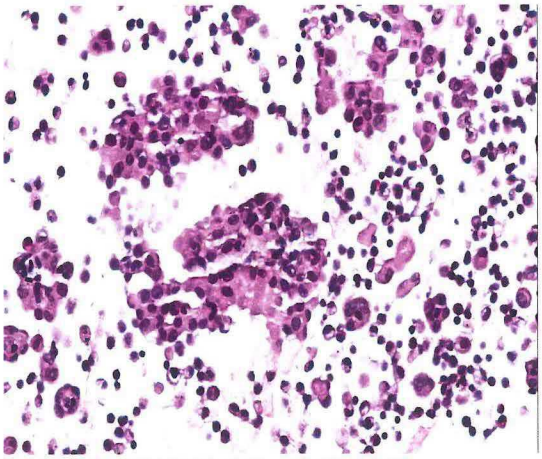

Fig. 9 – H&E(3) 360x (S-13-3878)

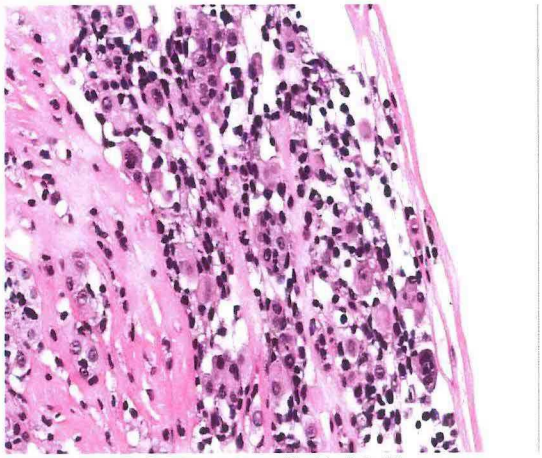

Fig. 10 – H&E(3) 360x (S-13-3878)

Illustrations

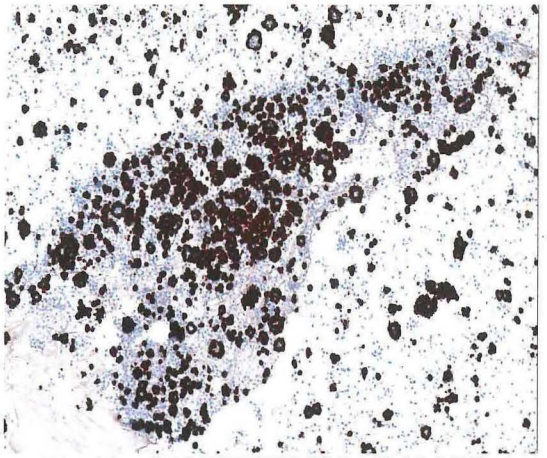

Fig. 11 – CALRETININ 90x (S-13-3878

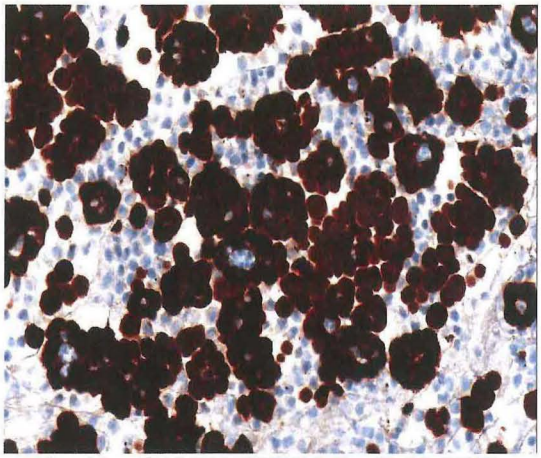

Fig. 12 – CALRETININ 360x (S-13-3878)

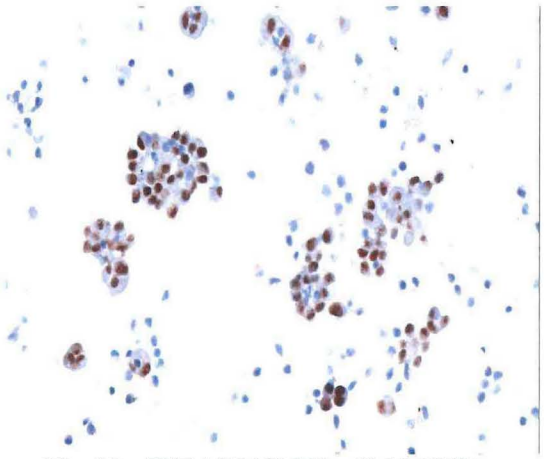

Fig. 13 – WT-1(2013) 360x (S-13-3878)

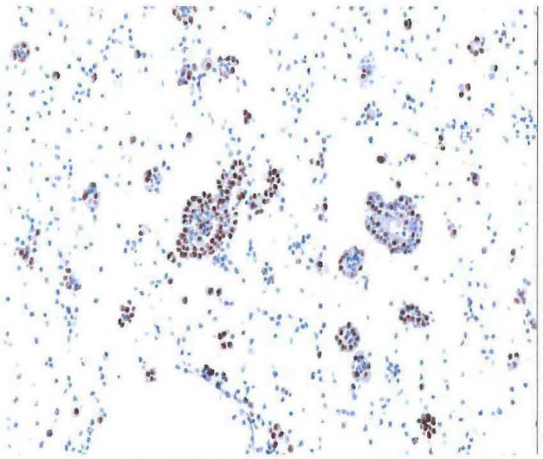

Fig. 14 – WT-1(2013) 180x (S-13-3878)

Fig. 15 – B-CATENIN 180x (S-13-3878)

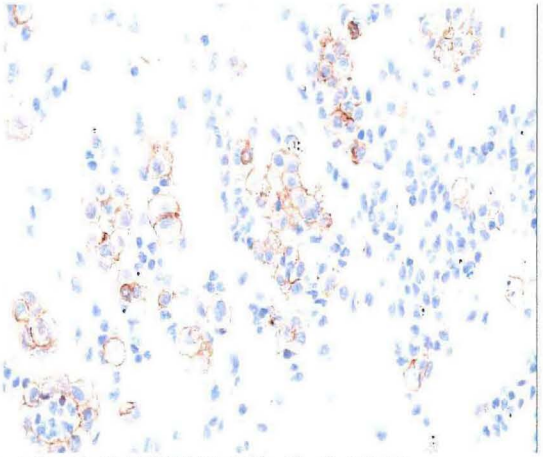

Fig. 16 – B-CATENIN 360x(S-13-3878)

Illustrations

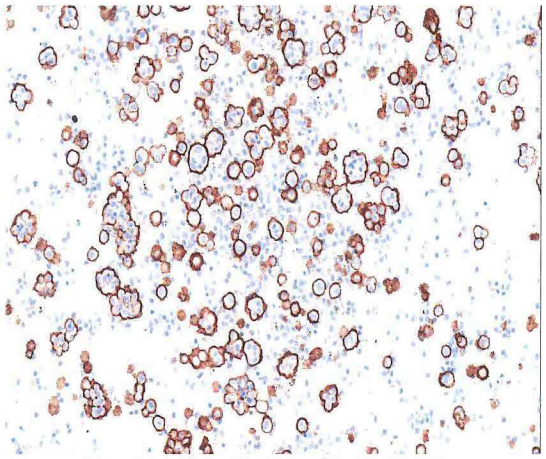

Fig. 17 – D2-40 180x (S-13-3878)

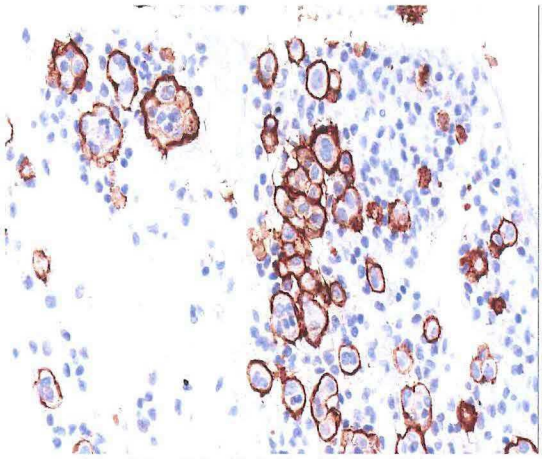

Fig. 18 – D2-40 360x (S-13-3878)